



Australian Government

Medical Services Advisory Committee

## Public Summary Document

### ***Application No. 1622 – Cardiac ablation devices for use in ventricular arrhythmia and supraventricular tachycardia***

**Applicant: Medical Technology Association of Australia (MTAA) on behalf of Abbott Medical, Boston Scientific Corporation, Johnson and Johnson Medical and Medtronic Australasia**

**Date of MSAC consideration: MSAC 79<sup>th</sup> Meeting, 28-29 July 2020**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, [visit the MSAC website](#)

#### **1. Purpose of application**

An application requesting extension of the current Prostheses List (PL) listing of cardiac ablation catheters and related technologies ('cardiac ablation devices') in patients with symptomatic ventricular arrhythmia (VA) or non-atrial fibrillation [AF] supraventricular tachycardia (non-AF SVT) was received from the Medical Technology Association of Australia (MTAA) on behalf of Abbott Medical, Boston Scientific Corporation, Johnson and Johnson Medical and Medtronic Australasia by the Department of Health.

#### **2. MSAC's advice to the Minister**

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC supported a recommendation to the Prostheses List Advisory Committee (PLAC) to expand the use of cardiac ablation catheters to include treatment of symptomatic ventricular arrhythmia (VA) and non-atrial fibrillation supraventricular tachycardia (non-AF SVT), based on safety, efficacy and likely cost-effectiveness. MSAC recommended that a patient registry be developed to capture the performance of individual practitioners and laboratories to monitor patient outcomes.

#### **Consumer summary**

This application is from the Medical Technology Association of Australia on behalf of Abbott Medical, Boston Scientific Corporation, Johnson and Johnson Medical and Medtronic Australasia. The application seeks to extend the use of cardiac ablation catheters to include treatment of symptomatic ventricular arrhythmia (VA) and non-atrial fibrillation supraventricular tachycardia (non-AF SVT). The Prostheses List Advisory Committee (PLAC <https://www1.health.gov.au/internet/main/publishing.nsf/Content/health-about-PLAC>) has sought MSAC's advice in relation to this request.

## Consumer summary

Cardiac ablation catheters are flexible thin wires that are inserted through the blood vessels to the heart to stop irregular electrical signals in the heart tissue that can cause arrhythmias (regular or irregular and often rapid heartbeat). Four Medical Benefits Schedule (MBS) items for services relating to catheter-based arrhythmia ablation of atrial fibrillation, VA and non-AF SVT) have been listed since 1998. However, the current Prostheses List (<https://www1.health.gov.au/internet/main/publishing.nsf/Content/health-privatehealth-prostheseslist.htm>) only covers private health insurance funding for ablation in patients with AF. This application seeks to amend the Prostheses List to include use of these devices in all cardiac ablation procedures.

MSAC found there was enough evidence to show that the use of cardiac ablation catheters was safe and effective in treating VA and non-AF SVT.

### **MSAC's advice to the Commonwealth Minister for Health**

MSAC advised PLAC to expand the use of cardiac ablation catheters to include treatment of VA and non-AF SVT, based on safety, efficacy and likely cost-effectiveness.

## **3. Summary of consideration and rationale for MSAC's advice**

MSAC noted that this is a fit-for-purpose application requesting the extension of the current Prostheses List (PL) listing of cardiac ablation catheters to include treatment of patients with symptomatic VA or non-AF SVT. The assessment report seeks to extend PL listing for cardiac ablation devices to all four existing MBS items (38290, 38287, 38293 and 38518) with the current PL "bundled price" of \$6,399 for ablation devices.

MSAC noted that there is only a small number of systematic reviews and randomised control trials and that this is a potential source of bias. On the basis of the identified clinical evidence, it is suggested that relative to no ablation, cardiac ablation has superior safety and superior effectiveness for all of the proposed patient groups in this application.

MSAC noted that catheter ablation is likely to have superior safety compared with anti-arrhythmic drugs.

In terms of clinical effectiveness, for non-AF SVT, catheter ablation is effective in reducing arrhythmia recurrence. The outcome of VA recurrence was not statistically significant when evidence from conference abstracts were excluded, but overall, MSAC accepted the likelihood of effectiveness in this population.

MSAC noted that the economic model did not allow for crossover from medical therapy to ablation; in practice, if medical therapy or ablation is unsuccessful the patient can proceed to ablation, or re-ablation, respectively as standard practice.

MSAC noted that a weighted incremental cost-effectiveness ratio (ICER) was not appropriate for this application because of the different time horizons used. MSAC queried whether PLAC would want to consider separate ICERs depending on indication of use, or a single weighted ICER. However, MSAC agreed that for the sake of transparency it was important for PLAC to be able to consider the separate ICERs for VA, atrial flutter and all remaining tachycardia groups.

MSAC noted that a key uncertainty is whether the exclusion of VA and non-AF SVT from the current PL listing means: that some patients are not receiving cardiac ablation, if those that are having ablation are paying significant out-of-pocket expenses, or whether patients who could otherwise be managed in private hospitals currently undergo the procedure in public hospitals. The MBS data only provide an estimate of current private sector utilisation, and as current private health insurance subsidies for cardiac ablation for VA and SVT are unknown, the net impact of extending the current PL listing is therefore highly uncertain.

MSAC noted that the applicant's pre-MSAC response was not in favour of making a registry a condition of listing VA and non-AF SVT on the PL because it is not for a new or amended item. However, MSAC agreed with the Evaluation Sub-committee's suggestion of a registry, which should be consistent with the Australian Commission on Safety and Quality in Health Care's Framework on Australian clinical quality registries, and that industry should be a key stakeholder.

#### **4. Background**

In October 2017, the Minister for Health, the Hon Greg Hunt MP requested an assessment of comparative clinical and cost-effectiveness from the PLAC regarding the inclusion of cardiac ablation catheters for atrial fibrillation (AF) on the PL. Consumer groups had previously claimed that affordable access to cardiac ablation is limited in Australia and including this procedure on the PL would therefore provide more certain access to appropriately insured patients.

A fit-for-purpose approach was used to assess the technology, culminating in [three assessment reports](#) (collectively referred to in the applicant developed assessment report [ADAR] as the 'AF Review'): a rapid review of high-level clinical evidence to address two very specific clinical questions; a focused economic evaluation and financial analysis; and an extended economic analysis.

At its November 2018 meeting, MSAC considered cardiac ablation catheters for the treatment of AF ([Final MSAC minutes - November 2018](#)). In summary, MSAC advised that catheter ablation for AF is not cost-effective at the current catheter prices and based on other assumptions in the economic analysis. MSAC suggested there should be further consideration following updated economic modelling using respecified outcomes and inputs (e.g. 10-year time horizon, repeat procedure rates based on MBS data, not including stroke reduction, and better determining the number and mix of catheters used per procedure).

The evaluation was presented to the MSAC Executive and the PLAC to inform consideration of a cost-effective benefit at which to list cardiac ablation devices for the treatment of AF. At its February 2019 meeting, the MSAC Executive advised that cardiac ablation catheters are likely to be cost-effective over a ten-year time horizon at a bundled price (incorporating ablation and mapping catheters and patches) [[Final MSAC minutes – February 2019](#)].

In March 2019, cardiac ablation catheters and related technologies (mapping catheters and patches), collectively referred to as 'cardiac ablation devices,' were included on Part C of the PL for the treatment of AF procedures covered by MBS item 38290. In November 2019, the listings were extended to procedures covered by MBS item 38287, where the procedure is for the treatment of AF.

The current PL (Part C) condition for cardiac ablation devices is:

*“The prosthesis is only to be used in a surgical procedure described in item 38290 or 38287 in Group T8 of the Health Insurance (General Medical Services Table) Regulations 2018 AND where the procedure is for the treatment of atrial fibrillation.”*

The MTAA has communicated, on behalf of sponsor companies, that many PHIs have subsequently stopped ex gratia payments for cardiac ablation devices for other arrhythmias, including those covered by existing MBS service items.

## **5. Prerequisites to implementation of any funding advice**

The ADAR stated that the cardiac ablation devices relevant to this application are all included on the Australian Register of Therapeutic Goods (ARTG). The ADAR stated that the Therapeutic Goods Administration (TGA)-registered intended purpose of some of these cardiac ablation devices is for management of a range of cardiac arrhythmias, not just atrial fibrillation.

## **6. Proposal for public funding**

Cardiac ablation devices are included in the current PL (Part C), but the listing is tied to MBS item 38290 (which is specific to treatment of AF) or 38287 “where the procedure is for the treatment of AF”. The ADAR seeks to extend the PL listing for cardiac ablation devices to all indications covered by the four existing MBS items (38290, 38287, 38293 and 38518) for catheter-based arrhythmia ablation services. The ADAR does not seek new MBS item numbers or seek to amend existing MBS item numbers.

The proposal is that the current PL ‘bundled price’ of \$6,399 for cardiac ablation devices for the AF indication will be maintained across all indications.

## **7. Summary of public consultation feedback/consumer issues**

The ADAR was accompanied by supporting letters from one specialist organisation and one other organisation. The letters reiterate the negative impact of VT, non-AF SVT and implantable cardioverter defibrillator (ICD) shocks on quality of life, and the long waiting lists for ablation procedures at public hospitals.

## **8. Proposed intervention’s place in clinical management**

### **Description of Proposed Intervention**

Cardiac ablation catheters are used in minimally invasive procedures in which a cardiac electrophysiologist advances a flexible thin wire (the catheter) through the blood vessels to the heart to ablate the muscle that initiates or conducts abnormal electrical signals in the heart tissue (arrhythmias). The procedure involves radiofrequency catheter ablation (RFCA) or cryoablation.

## **Description of Medical Condition(s)**

The populations requiring curative ablation procedures, for whom expansion of the PL listing for cardiac ablation devices is sought are patients with symptomatic VA or non-AF SVT. There are two main types of VA: ventricular tachycardia (VT) and ventricular fibrillation (VF). The ADAR notes a range of distinct SVT types: sinus tachycardia, atrial tachycardia (AT), macro re-entrant atrial tachycardia (MART, commonly referred to as atrial flutter [AFL]), atrioventricular nodal re-entrant tachycardia (AVNRT), symptomatic atrioventricular reciprocating tachycardia (AVRT, which includes Wolff-Parkinson-White syndrome), focal junctional ectopic tachycardia and non-paroxysmal junctional tachycardia.

## **Place in clinical management**

### *Ventricular arrhythmia*

The ADAR stated that there are no Australian guidelines for the treatment of VA. However, the: European Society of Cardiology 2019 guidelines on catheter ablation of VA (Cronin 2019<sup>1</sup>), which supplement the 2017 American Heart Association (AHA)/ American College of Cardiology (ACC)/ Heart Rhythm Society (HRS) guidelines and the 2015 European Society of Cardiology guidelines for the management of patients with VA (Al-Khatib 2018<sup>2</sup>, Priori 2015<sup>3</sup>), each strongly recommend cardiac ablation for treatment of symptomatic VA in comparison to anti-arrhythmic drug (AAD) therapy. The key opinion leader (KOL) advised that the European Society of Cardiology and ACC/HRS guidelines are those followed by clinicians in Australia.

The ADAR stated that prior to, or following ablation, patients with VA and the following conditions may undergo ICD implantation:

- documented VF, or VT which is not haemodynamically tolerated and in the absence of reversible causes, or within 48 h after myocardial infarction (MI) who are receiving chronic optimal medical therapy
- recurrent sustained VT (not within 48 hours after MI) who are receiving chronic optimal medical therapy, have a normal left ventricular ejection fraction (LVEF).

The European Society of Cardiology clinical algorithm for patients with VT and ischaemic heart disease (IHD) including cardiac ablation is presented in Figure 1. The ADAR stated this shows that for patients with an ICD who have recurrent ICD therapies in response to ongoing VT, cardiac ablation is recommended. In the hypothetical absence of cardiac ablation, the KOL advised that patients would receive AADs (not shown in Figure 1) but as mentioned above, cardiac ablation is recommended practice).

The Commentary stated that the algorithm presented in the ADAR was for congenital VA, which may be applicable to the broader acquired IHD population, but no justification was

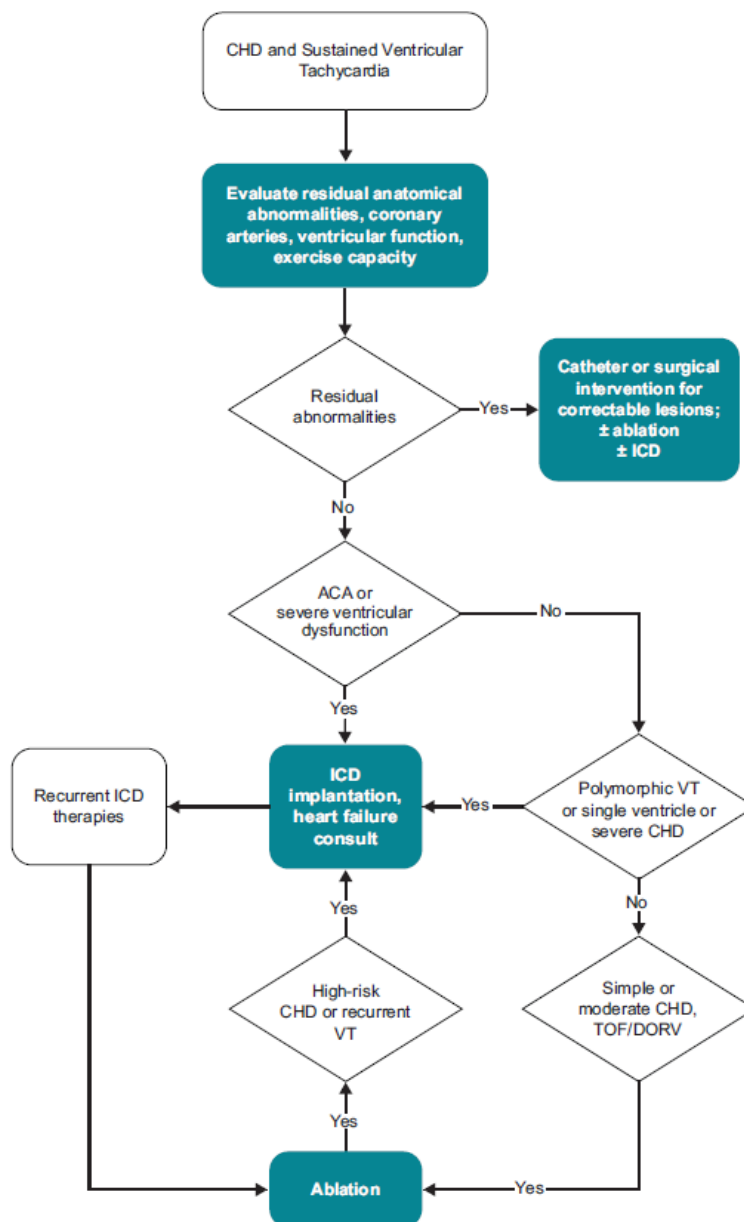
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<sup>1</sup> Cronin, EM, Bogun, FM, Maury, P, et al. (2019). "2019 HRS/EHRA/APHRS/LAHRs expert consensus statement on catheter ablation of ventricular arrhythmias." *EP Europace*, 21(8): 1143-1144.

<sup>2</sup> Al-Khatib, SM, Stevenson, WG, Ackerman, MJ et al. (2018). 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death. A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society, 138: e272–e391

<sup>3</sup> Priori, SG, Blomstrom-Lundqvist, C, Mazzanti, A, et al. (2015). "2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC)." *Eur Heart J*, 36(41): 2793-2867.

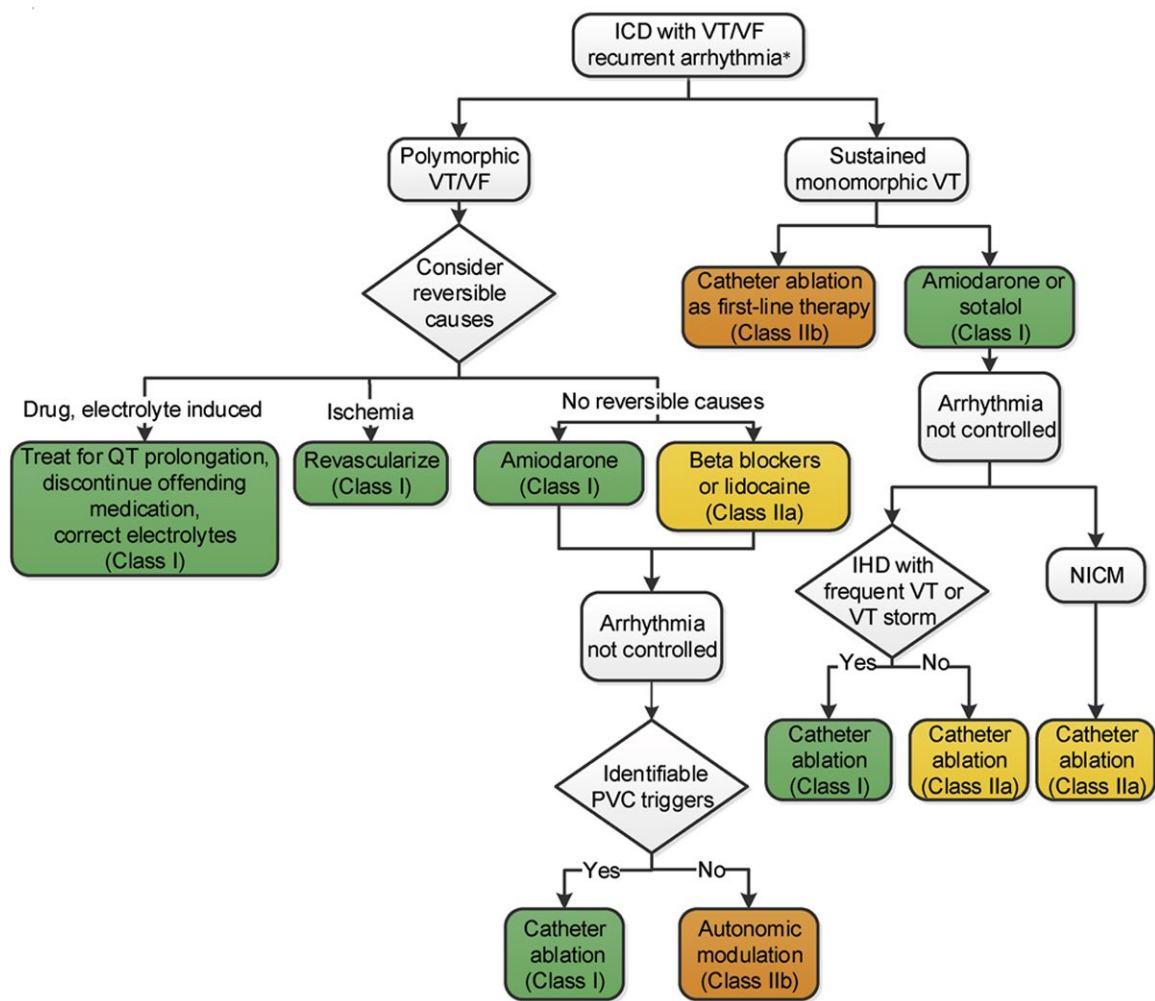
provided in the ADAR to support this. An alternative clinical management algorithm is presented for patients with an ICD (Figure 2) and without an ICD (Figure 3).



**Figure 1 Clinical management algorithm for VT and IHD with and without an ICD**

Source: Cronin 2019 (Figure 2, p.1144x)

ACA, aborted cardiac arrest; CHD, congenital heart disease (same as ischaemic heart disease); DORV, double outlet right ventricle; ICD, implantable cardioverter defibrillator; TOF, tetralogy of Fallot; VT, ventricular tachycardia



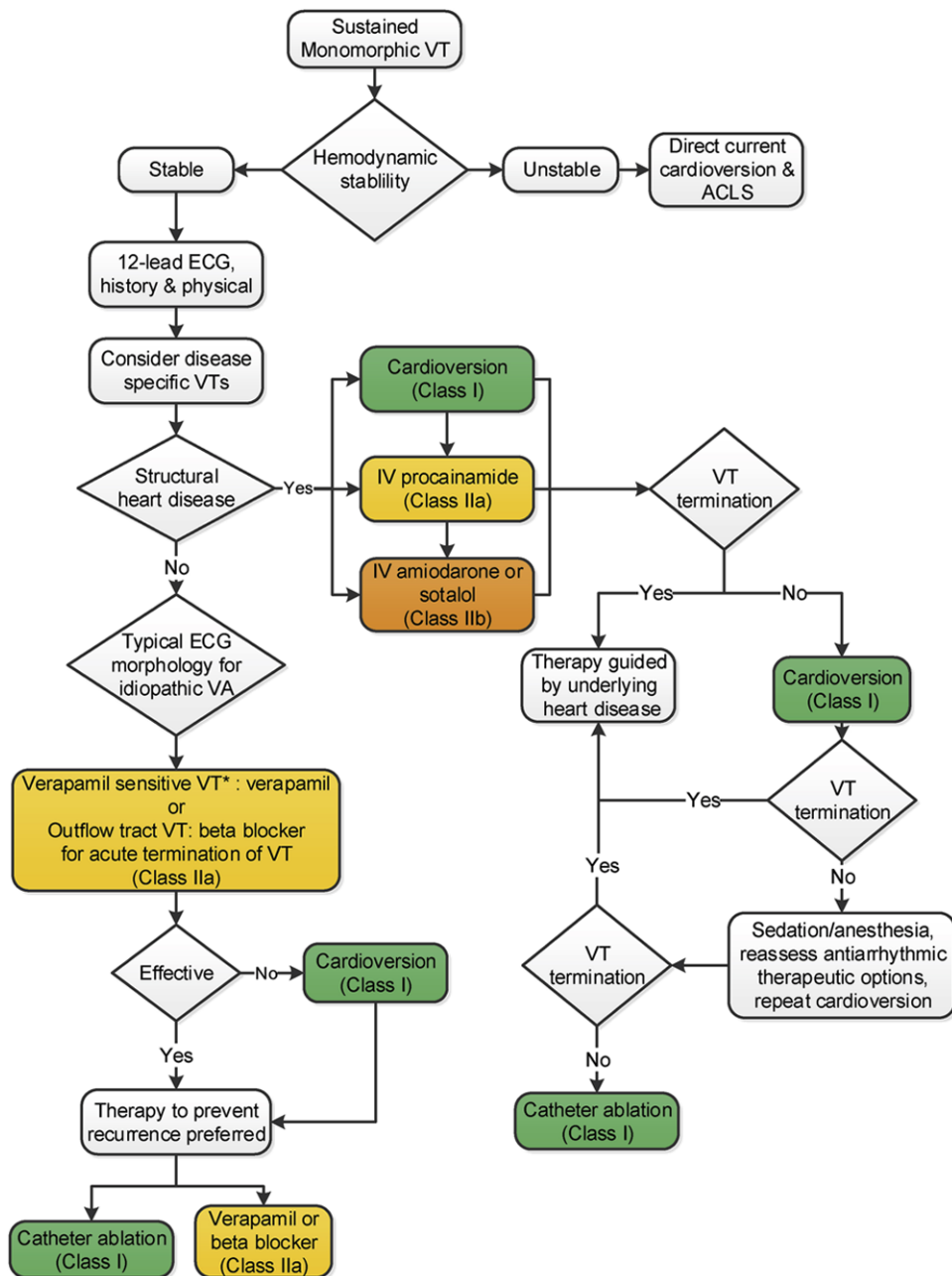
**Figure 2 Clinical management algorithm for recurrent VA in patients with an ICD**

Source: Al-Khatib 2017 (figure 5, e306)

Colours correspond to Class of Recommendation.

\* Management should start with ensuring that the ICD is programmed appropriately and that potential precipitating causes, including heart failure exacerbation, are addressed

PHRS=Asia Pacific Heart Rhythm Society; EHRA=European Heart Rhythm Association; HRS=Heart Rhythm Society; IHD=ischaemic heart disease; ICD=implantable cardioverter defibrillator; PVC=premature ventricular complex; NICM=nonischemic cardiomyopathy; VF=ventricular fibrillation; VT=ventricular tachycardia.



**Figure 3 Clinical management algorithm for sustained monomorphic VT**

Source: Al-Khatib 2017 (figure 2, e300)

Colours correspond to Class of Recommendation.

ACLS=advanced cardiovascular life support; ECG=electrocardiogram; VA=ventricular arrhythmia; VT=ventricular tachycardia.

### *Supraventricular tachycardia*

The ADAR stated there are no Australian guidelines for the treatment of SVT. However, the 2019 European Society of Cardiology guidelines for the management of SVT recommend cardiac ablation as first-line treatment for symptomatic and recurrent SVT (particularly atrioventricular nodal re-entrant tachycardia [AVNRT]) because it substantially improves quality of life (QoL) and reduces costs (Brugada 2019<sup>4</sup>). If cardiac ablation is not desirable or feasible, then AADs should be considered.

<sup>4</sup> Brugada, J, Katritsis, DG, Arbelo, E, et al. (2019). "2019 ESC Guidelines for the management of patients with supraventricular tachycardia: The Task Force for the management of patients with supraventricular tachycardia of the European Society of Cardiology (ESC)." *Eur Heart J*, 00: 1-65.



The European Society of Cardiology clinical management algorithms for management of AFL and AVNRT, including use of cardiac ablation, are presented in Brugada 2019 (Figure 12 and Figure 15). These figures show that for patients with symptomatic and recurrent AFL or AVNRT cardiac ablation is recommended either as first-line treatment or where AADs are either ineffective or undesirable. In the hypothetical absence of cardiac ablation, the KOL advised that patients would only have the option of AADs. Anticoagulant therapy, such as warfarin and aspirin, may be given to patients following cardiac ablation for VA or SVT for a limited period of time, at the discretion of the treating physician, to minimise the risk of thromboembolic complications (Brugada 2019, Cronin 2019).

The Commentary stated that the clinical algorithms for AFL and AVNRT are clear and appropriate and show that in the absence of catheter ablation, the appropriate therapy would be drug based, although catheter ablation is recommended as first-line treatment in symptomatic patients with recurrent episodes.

## 9. Comparator

The comparator for cardiac ablation for the treatment of VA and non-AF SVT has been broadly defined in the ADAR as ‘no cardiac ablation,’ which includes medical treatment with AADs.

The Commentary considered that the comparator is appropriate and may be partially, but not completely, replaced by catheter ablation as it is possible for patients to still require AADs after ablation. Although ICD implantation and cardioversion are management options for the populations of interest, they are not considered comparators for catheter ablation.

## 10. Comparative safety

### *Ventricular arrhythmia*

Four systematic literature reviews (SLRs) were included in the ADARs synthesis of high-level clinical evidence for the VA population (Anderson 2019<sup>5</sup>, Atti 2018<sup>6</sup>, Martinez 2019<sup>7</sup> and Tilz 2019<sup>8</sup>; see Table 1). Collectively these SLRs included eight RCTs, including five full papers and three conference abstracts.

The Commentary stated that the Martinez (2019) SLR is considered to be of moderate quality and should be used in preference to the Anderson SLR as the basis of the clinical assessment (Table 1). The Commentary also considered that the two other SLRs are of ‘low’ quality and also less applicable as they excluded studies where AADs were used in the comparator arm. These SLRs are excluded from further consideration in the Commentary (~~striketrough~~ below). The Commentary also considered a key difference between the Anderson (2019) and Martinez (2019) SLRs is in how they have defined recurrence and which studies have been included for this outcome. The Anderson SLR has included studies that specifically measured recurrence, as well as those that included ‘appropriate ICD events.’ The Martinez SLR has

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<sup>5</sup> Anderson, RD, Ariyaratna, N, Lee, G, et al. (2019). "Catheter ablation versus medical therapy for treatment of ventricular tachycardia associated with structural heart disease: Systematic review and meta-analysis of randomized controlled trials and comparison with observational studies." *Heart Rhythm*, 16(10): 1484-1491.

<sup>6</sup> Atti, V, Vuddanda, V, Turagam, MK, et al. (2018). "Prophylactic catheter ablation of ventricular tachycardia in ischemic cardiomyopathy: a systematic review and meta-analysis of randomized controlled trials." *J Interv Card Electrophysiol*, 53(2): 207-215.

<sup>7</sup> Martinez, BK, Baker, WL, Konopka, A, et al. (2019). "Systematic review and meta-analysis of catheter ablation of ventricular tachycardia in ischemic heart disease." *Heart Rhythm*, 0: 1547-5271

<sup>8</sup> Tilz, RR, Eitel, C, Lyan, E, et al. (2019). "Preventive Ventricular Tachycardia Ablation in Patients with Ischaemic Cardiomyopathy: Meta-analysis of Randomised Trials." *Arrhythm Electrophysiol Review*, 8(3): 173-179.

only included the studies that specifically measured recurrence and a separate analysis was undertaken for ‘appropriate ICD events.’

**Table 1 Results from the systematic reviews and trials – peri-procedural complications**

Study ID Risk of bias	Population (follow-up)	No. studies	Definition	Cardiac ablation n/N (%)	No ablation n/N (%)	Risk estimate (95% CI)	Heterogeneity P-value; I <sup>2</sup>
Anderson 2019 <del>Moderate</del> <del>Low</del> quality <sup>h</sup>	VT+IHD+ICD (mean 22 months, range 6-27.9 months) <sup>b</sup>	7 RCTs <sup>a</sup>	Major procedural complications	8.3% (95% CI: 5.6%, 12.2%)	NR	NR	p-value NR, I <sup>2</sup> =18%
Atti 2018 <del>Low</del> quality <sup>h</sup>	VT+IHD+ICD (mean 24.1, range 22.5-27.9 months) <sup>b</sup>	3 RCTs <sup>c</sup>	Major AEs	25/170 (14.7%)	19/176 (10.8%)	OR 1.45 (0.52, 4.01), p=0.47	p=0.18; I <sup>2</sup> =43%
Martinez 2019 <del>Moderate</del> quality <sup>h</sup>	VT+IHD+ICD (mean 24.9, range 6-27.9 months) <sup>b</sup>	5 RCTs <sup>d</sup>	Procedural-related AEs <sup>f</sup>	30/315 (9.5%)	NR	NR	NR
Tilz 2019 <del>Low</del> quality <sup>h</sup>	VT+IHD+ICD (mean 24.1, range 22.5-27.9 months) <sup>b</sup>	3 RCTs <sup>c</sup>	Major complications	24/170 (14.1%)	19/176 (10.8%)	OR 1.39 (0.43, 4.51), p=0.584	p=0.118; I <sup>2</sup> =53.3%
Da Costa 2006 Satisfactory quality <sup>g</sup>	AFL (mean 13 months)	1 RCT	Complications	0/52 (0%)	5/52 (9.6%)	<b>RD -9.6% (- 17.6%, - 1.6%)<sup>e</sup>; p=0.03</b>	-

Source: Table 29 (p.63) of the ADAR, with Commentary amendments. Low applicability studies, and Commentary suggested changes, are indicated with a strikethrough.

AE=adverse event; AFL=atrial flutter; AVNRT=atrioventricular nodal re-entrant tachycardia; CI=confidence interval; ICD=implantable cardioverter defibrillator; IHD=ischaemic heart disease; NR=not reported; OR=odds ratio; RCT=randomised controlled trial; RR=relative risk; VT=ventricular arrhythmia

a Al-Khatib 2015, Epstein 1998, Koa-Wing 2009, Kuck 2010, Kuck 2017, Reddy 2007, Sapp 2016

b Calculated mean follow-up for RCTs by weighting mean follow-up period by each RCT by sample size

c Kuck 2010, Kuck 2017, Reddy 2007

d Al-Khatib 2015, Kuck 2010, Kuck 2017, Reddy 2007, Sapp 2016

e Risk difference calculated for the ADAR

f Adverse events not reported in the control arms due to variations in control strategies; however, SLR concluded AEs were less common in the ablation arm versus the AAD arm

g Assessed in the SLR by the Centre for Reviews and Dissemination, University of York UK (Rodgers 2008, Appendix 2)

h Calculated using the AMSTAR 2 tool (Shea 2017), see Section B.3 of the ADAR.

Statistically significant results are in **bold** text (p-value <0.05).

The Martinez (2019) SLR reported a statistically significant reduction in cardiac hospitalisation for patients undergoing cardiac ablation (odds ratio [OR] 0.67; 95% CI 0.46, 0.97) over a mean follow-up period of 25.5 months (Table 2).

**Table 2 Results from the systematic reviews and trials – cardiac hospitalisation**

Study ID Quality	Population (follow-up)	No. studies	Cardiac ablation n/N (%)	No ablation n/N (%)	Risk estimate (95% CI) p-value	Heterogeneity P-value; I <sup>2</sup>
Martinez 2019 Moderate quality <sup>f</sup>	VT+IHD+ICD (mean 25.5 months) <sup>a</sup>	4 RCTs <sup>b</sup>	76/249 (30.5%)	101/253 (39.9%)	<b>OR 0.67 (0.46, 0.97)</b> p-value NR	p=0.56; I <sup>2</sup> =0%
Natale 2000 Satisfactory quality <sup>d</sup>	AFL (mean 22 months)	1 RCT	7/31 (22.6%)	19/30 (63.3%)	<b>RR 0.36 (0.18, 0.72)<sup>c</sup></b> p<0.01	NA
Katritsis 2017 Satisfactory quality <sup>e</sup>	AVNRT (60 months)	1 RCT	0/30 (0%) 0/29 (0%)	21/31 (67.7%) 21/28 (75%)	<b>RD -67.7% (-84.2%, - 51.3%)</b> p<0.01 <sup>g</sup>	NA

Source: Table 27 (p.60) of the ADAR. *Commentary changes in blue text.*

AFL=atrial flutter; AVNRT=atrioventricular nodal re-entrant tachycardia; CI=confidence interval; ICD=implantable cardioverter defibrillator; IHD=ischemic heart disease; NA = not applicable; NR=not reported; OR=odds ratio; RCT=randomised controlled trial; VT=ventricular tachycardia.

a Calculated mean follow-up for 4 RCTs by weighting mean follow-up period by each RCT by sample size

b Al-Khatib 2015, Kuck 2010, Kuck 2017, Sapp 2016

c Relative risk calculated for the ADAR

The rate of repeat ablation were not reported in the SLRs, but individual RCTs included in the ADAR reported rates ranging from 6% to 15% over two years from the index ablation procedure.

### *Supraventricular tachycardia*

Of the three RCTs in SVT populations, only one reported complication rates (Table 1).

Da Costa (2006<sup>9</sup>) found a statistically significantly lower rate of complications for patients with AFL undergoing cardiac ablation (0% vs. 9.6%, p=0.03). The rate of repeat ablations in an AFL population at mean 22 months' follow-up was 6.4%.

The Commentary stated that there is very limited evidence provided to assess safety in the SVT populations. Hospitalisations reported in the SVT population are arrhythmia specific and considered an effectiveness outcome rather than a safety outcome (Table 2). Procedural complication rates reported in clinical practice guidelines are lower than for VA and, although they differed by population, support superior safety for catheter ablation compared to AADs.

## **11. Comparative effectiveness**

### *Ventricular arrhythmia*

The Commentary summarised comparative effectiveness using data from the Martinez (2019) SLR, as this is the highest quality SLR and the outcomes are clearly defined (Table 3). The Commentary considered that:

- there is not convincing evidence that cardiac ablation reduces all-cause mortality or recurrence of VT/VF in patients with an ICD
- there is convincing evidence that cardiac ablation reduces appropriate ICD therapies and electrical storm. Although these outcomes were not specified in the PICO, they

<sup>9</sup> Da Costa, A, Thevenin, J, Roche, F, et al. (2006). "Results from the Loire-Ardeche-Drome-Isere-Puy-de-Dome (LADIP) trial on atrial flutter, a multicentric prospective randomized study comparing amiodarone and radiofrequency ablation after the first episode of symptomatic atrial flutter." *Circulation*, 114(16): 1676-1681.

are patient relevant and reflect (any) arrhythmia recurrence but at a lower threshold based on ICD programming.

**Table 3 Results of Martinez (2019) meta-analysis across the key outcomes**

Study ID No. of RCTs	Risk of bias	Intervention n with event/N (%)	Comparator n with event/N (%)	Relative difference OR (95% CI)	I <sup>2</sup> statistic
<b>All-cause mortality</b>					
Martinez 2019 5 RCTs	Moderate quality	58/315 (18.4%)	63/317 (19.9%)	OR 0.89 (0.60, 1.34)	I <sup>2</sup> =0%, p=0.79
<b>Arrhythmia recurrence</b>					
Martinez 2019 3 RCTs	Moderate quality	61/119 (51.3%)	71/126 (56.3%)	OR 0.87 (0.41, 1.85)	I <sup>2</sup> =44%, p=0.17
<b>Appropriate ICD therapies</b>					
Martinez 2019 3 RCTs	Moderate quality	54/170 (31.8%)	83/176 (47.2%)	<b>OR 0.49 (0.28, 0.87)</b>	I <sup>2</sup> =32%, p=0.23
<b>Electrical storm</b>					
Martinez 2019 4 RCTs	Moderate quality	59/302 (19.5%)	82/303 (27.1%)	<b>OR 0.64 (0.43, 0.95)</b>	I <sup>2</sup> =0%, p=0.57

Source: Table 1, pxiv of the Commentary

CI=confidence interval; ICD=implantable cardioverter defibrillator; OR=odds ratio; RCT=randomised controlled trial.

Statistically significant results are in **bold** text (p-value <0.05)

However, in the pre-Evaluation Sub-Committee response the applicant considered Anderson (2019) to provide a more accurate assessment of the overall efficacy of cardiac ablation in preventing future recurrences of VT compared with no ablation:

- Anderson (2019) includes 787 patients across 8 studies, whereas Martinez (2019) includes only 632 patients over 5 studies
- Anderson (2019) uses a broader definition of VT recurrence<sup>10</sup>, including appropriate ICD shocks and therapies As noted in the Commentary, ICD shocks and therapies “are likely to be relevant (to patients with VT) and to impact on quality of life”. On the basis of this pooled clinical evidence, Anderson (2019) reported a statistically significant reduction in VT recurrence with cardiac ablation vs no ablation (relative risk [RR] 0.78, 95% confidence interval [CI]: 0.64, 0.95)
- ICD therapies are a subset of all VT recurrences, and the use of ICD therapies as a proxy for VT recurrences by Anderson (2019) will likely under-estimate the rates of all VT recurrences and therefore the relative efficacy of cardiac ablation. Despite this, Anderson (2019) reported a statistically significant 22% reduction in VT recurrence with cardiac ablation as noted above
- VT storm is a distinct arrhythmic emergency and highly malignant condition experienced by up to 40% of ICD recipients during their lifetime (Looi 2015<sup>11</sup>). Recurrent ICD shocks increase mortality (Poole 2008<sup>12</sup>), most commonly due to rapid and progressive deterioration in ventricular function and consequent heart failure (Looi 2015), and VT storm is associated with an 18-fold increase increased risk of

<sup>10</sup> The sponsors agree that ICD therapies, ICD shocks and VT storm are important outcomes for patients with VA. As explained above, these outcomes are included within the assessment of ‘VT recurrence’ by Anderson (2019).

<sup>11</sup> Looi KL, Tang A, Agarwal S, et al, 2015, Ventricular arrhythmia storm in the era of implantable cardioverter-defibrillator, *Postgrad Med J*; 91: 519-526.

<sup>12</sup> Poole JE, Johnson GW, Hellkamp JA, et al, 2008, Prognostic importance of defibrillator shocks in patients with heart failure, *N Engl J Med*; 359: 1009-1017.

death (Sesselberg 2007<sup>13</sup>). Moreover, after an initial episode, recurrent VT storm occurs in 50-81% of patients over the next year. Multiple ICD shocks cause substantial psychological morbidity and markedly impaired quality of life (Passman 2007<sup>14</sup>), and have long-lasting adverse effects on physical activity, quality of life and anxiety (Sears 2018<sup>15</sup>). As a consequence, VT storm often results in exponential healthcare resource use from prolonged hospital stays and repeat clinic visits (Looi 2015, Winterfield 2018<sup>16</sup>)

- Observational data show cardiac ablation results in acute suppression of VT storm and long-term freedom from recurrent VT in 72% of patients (Nayyar 2013<sup>17</sup>).

Therefore, the applicant considered there is clear evidence demonstrating significant reductions in the components of VT recurrence (risks of ICD shocks/therapies and VT storm) with cardiac ablation.

### *Supraventricular tachycardia*

#### AFL

The key outcome reported in the ADAR was AFL recurrence, which was statistically significantly lower in the catheter ablation arms in both RCTs. The key outcome summarised in Table 4 is recurrence of any arrhythmia. The commentary suggested this outcome because AFL can coexist with AF. The Commentary considered that there is convincing evidence that catheter ablation reduces arrhythmia recurrence. All-cause mortality favoured catheter ablation but was not statistically significant (and is underpowered).

**Table 4 Key outcomes for AFL from the included RCTs**

Study ID	Risk of bias	Intervention n with event/N (%)	Comparator n with event/N (%)	Relative difference RR (95% CI)
<b>All-cause mortality</b>				
Da Costa 2006	Satisfactory quality	6/52 (11.5%)	8/51 (15.7%)	RR 0.74 (0.27, 1.97) <sup>a</sup> p=0.7
<b>(any) Arrhythmia recurrence</b>				
Natale 2000	Satisfactory quality	6/31 (19.4%)	19/30 (63.3%)	<b>RR 0.31 (0.14-0.66)</b> <b>p&lt;0.001</b>

Source: Table 2, pxiv of the Commentary

AFL=atrial flutter; CI=confidence interval; RCT=randomised controlled trial; RR=risk ratio.

<sup>a</sup> Relative risk calculated for the ADAR.

Statistically significant results are in **bold** text (p-value <0.05)

#### AVNRT

The Commentary stated that the primary endpoint of the Katritsis (2017) RCT was hospital admission for persistent tachycardia cardioversion, during a follow-up period of 5 years. The

<sup>13</sup> Sesselberg HW, Moss A, McNitt S, et al, 2007, Ventricular arrhythmia storms in postinfarction patients with implantable defibrillators for primary prevention indications: A MADIT-II substudy, Heart Rhythm, 4(1), 1395-1402

<sup>14</sup> Passman R, Subacius H, Ruo B, et al, 2007, Implantable cardioverter defibrillators and quality of life: results from the defibrillators in nonischemic cardiomyopathy treatment evaluation study, Arch Intern Med; 167: 2226-2232.

<sup>15</sup> Sears SF, Rosman L, Sasaki S, et al, 2018, Defibrillator shocks and their effect on objective and subjective patient outcomes: results of the PainFree SST clinical trial, Heart Rhythm; 15(5): 734-740.

<sup>16</sup> Winterfield JR, Kent AR, Karst E, et al, 2018, Impact of ventricular tachycardia ablation on health care utilization, Heart Rhythm; 15(3): 355-362.

<sup>17</sup> Nayyar S, Ganesan AN, Brooks AG, et al, 2013, Venturing into ventricular arrhythmia storm: a systematic review and meta-analysis, Eur Heart J; 34(8): 560-571.

outcome is presented in Table 5. The Commentary considered that there is convincing evidence that cardiac ablation reduces arrhythmia recurrence in AVNRT.

**Table 5 Key outcomes for AVNRT from the included RCT**

Study ID	Risk of bias	Intervention n with event/N (%)	Comparator n with event/N (%)	Relative difference RD (95% CI)
<b>Arrhythmia recurrence – hospitalisation for cardioversion</b>				
Katritsis 2017	Satisfactory quality	0/30 (0%) 0/29 (0%) <sup>a</sup>	21/31 (67.7%) 21/28 (75%) <sup>a</sup>	<b>RD -67.7 (-84.2, -51.3)</b> <b>p&lt;0.01</b>

Source: Table 3, p xv of the Commentary

CI=confidence interval; RCT=randomised controlled trial; RD=risk difference. *Commentary changes in blue text.*

<sup>a</sup> Analysed population excluding patients lost to follow-up.

Statistically significant results are in **bold** text (p-value <0.05)

## Clinical claim

On the basis of the benefits and harms reported in Section B, the ADAR proposes that, relative to no ablation, catheter ablation has superior safety and superior effectiveness.

The Commentary considered that the clinical claim is reasonable:

- For the VA population: the claim is due to differences in ICD therapies, rather than ventricular arrhythmia recurrence per se. No evidence was presented for patients without an ICD
- For SVT populations, only three small RCTs were presented; however, due to the large magnitude of the effect, the evidence was judged convincing.

The Commentary noted no evidence was presented for non-AF SVT populations other than AFL and AVNRT. This means that catheter ablation for 30% of non-AF SVT (reportedly for accessory pathways or atrial tachycardia) is not represented within the evidence base informing the economic evaluation. However, an overview of studies informing clinical practice guidelines suggests effectiveness across all SVT populations.

In the pre-Evaluation Sub-Committee response, the applicant highlighted that:

- additional studies of cardiac ablation for other types of SVT presented in the Commentary Report “suggest similar rates of effectiveness” to those presented in the ADAR for AFL and AVNRT. In particular, an RCT reported by Pappone (2003<sup>18</sup>) found a statistically significantly lower rate of arrhythmic events at 5 years with cardiac ablation vs no ablation in patients with Wolff-Parkinson-White syndrome (WPWS) (RR 0.08; 95% CI: 0.02, 0.33; p <0.001)
- as per the KOL advice for this ADAR, idiopathic VT in the absence of structural heart disease represents approximately 30% of all cardiac ablation procedures performed for VA in Australia. No SLRs of RCTs for cardiac ablation in idiopathic VT were identified during the development of the ADAR. However, a prospective, randomised trial of 330 patients with frequent ventricular premature beats (VPBs) originating from the right ventricular outflow tract found significantly lower VPB recurrence at one year with cardiac ablation (19.4% vs. 88.6%; p < 0.001) and concluded that cardiac ablation is more efficacious than AADs for preventing VPB recurrence in these patients (Ling 2014<sup>19</sup>). The associated RR of 0.22 is substantially

<sup>18</sup> Pappone C, Santinelli V, Manguso F, et al, 2003, A randomized study of prophylactic catheter ablation in asymptomatic patients with the Wolff–Parkinson–White Syndrome, *N Engl J Med*; 349:1803-1811.

<sup>19</sup> Ling Z, Liu Z, Su L, et al, 2014, Radiofrequency Ablation Versus Antiarrhythmic Medication for Treatment of Ventricular Premature Beats from the Right Ventricular Outflow Tract Prospective Randomized Study, *Circ Arrhythm Electrophysiol*; 7: 237-243.

lower than estimated for patients with VT+IHD+ICD (0.78), which suggests that the efficacy of cardiac ablation may be even greater for patients with idiopathic VT

- a meta-analysis of six studies (including five uncontrolled studies) of cardiac ablation, including 70 patients with idiopathic VA, reports both a significant reduction in premature ventricular contractions (PVCs) in the 24 hours after cardiac ablation (mean reduction 30,089;  $p < 0.00001$ ), and a significant improvement in left ventricular ejection fraction (mean improvement 10.36%;  $p < 0.00001$ ), concluding that cardiac ablation improves cardiac function in these patients (Lamba 2014<sup>20</sup>). This evidence strongly supports cardiac ablation being more effective than medical therapy for idiopathic VA.

### Translation issues

The ADAR identified applicability, extrapolation and transformation issues, which were summarised by the Commentary (Table 6).

**Table 6 Translation issues identified in the ADAR**

Type	Issue
Applicability (Section C.2)	Applicability of the published SLRs/RCTs in Section B to the Australian patient population. <i>The evidence for VA is from SLRs of RCTs for VT conducted in Europe and North America, among patients predominantly with IHD and an ICD. The evidence for AFL is from two RCTs conducted in France and US/Italy. The evidence for AVNRT is from a single-centre RCT conducted in Greece that reported no recurrence among those undergoing cardiac ablation. The ADAR assesses the applicability of these results to an Australian setting.</i>
Extrapolation (Section C.3)	Extrapolation of the clinical evidence from the SLRs/RCTs over 10 years. <i>The time horizon of 10 years was selected primarily to align with the extended economic analysis in the AF Review, which was requested by MSAC following a focused economic analysis with a 1-year time horizon (consistent with the available RCT evidence for AF). Because the major costs for cardiac ablation are up-front, a shorter time horizon led to an increased ICER, which may unfairly underestimate the cost-utility in the longer-term. The trial evidence in the ADAR reported outcomes for VT+IHD+ICD to a maximum of 48 months follow-up, with a mean follow-up to 2 years. For SVT, follow-up was up to 22 months for AFL (though the trial used for the outcome of AFL recurrence had a mean follow-up of 13 months), and up to 5 years for AVNRT. Extrapolation of the trial evidence was required, and the ADAR has assumed recurrence continues at the same rate to 10 years for each of the three modelled non-AF conditions. For cardiac hospitalisation, the probability was considered to be equal for each arm beyond the trial data.</i>
Transformation (Section C.4)	Transformation of arrhythmia recurrence and cardiac hospitalisation to utility values. <i>The utility values assigned determine the incremental QALYs over the 10-year time horizon. The chosen health states needed to have disutility values assigned, with no relevant data reported in any of the assessed RCTs. Alternate sources were required for these values.</i>

Source: Table 21, p56 of the Commentary

ADAR=applicant developed assessment report; AFL=atrial flutter; AVNRT=atrioventricular nodal re-entrant tachycardia; ICD=implantable cardioverter defibrillator; ICER=incremental cost-effectiveness ratio; IHD=ischaeamic heart disease; MSAC=Medical Services Advisory Committee; QALY, quality-adjusted life year; RCT=randomised controlled trial; SLR=systematic literature review; SVT=supraventricular tachycardia; US=United States; VA=ventricular arrhythmia; VT=ventricular tachycardia.

## 12. Economic evaluation

The ADAR stated that the structure of the economic evaluation and model are consistent with the AF Review (Table 7).

<sup>20</sup> Lamba J, Redfearn DP, Michael KA, et al, 2014, Radiofrequency catheter ablation for the treatment of idiopathic premature ventricular contractions originating from the right ventricular outflow tract: A systematic review and meta-analysis; 37 (1): 73-8.

**Table 7 Summary of the economic evaluation**

<b>Perspective</b>	Health care payer
<b>Comparator</b>	No ablation, defined as AADs only (plus ICD implantation for VT+ICD+IHD patients)
<b>Type of economic evaluation</b>	Cost-utility analysis
<b>Sources of evidence</b>	VT+IHD+ICD patients: systematic review and meta-analysis of RCTs AFL and AVNRT patients: individual RCTs
<b>Time horizon</b>	10 years
<b>Outcomes</b>	QALYs
<b>Methods used to generate results</b>	Hypothetical cohort of 1,000 people aged 61-70 years (VT+IHD+ICD patients; AFL patients) or 41-50 years (AVNRT patients) for each arm based on the mean ages of trial patients and mean ages estimated by the KOL. The cohort remains in this age bracket for the duration of the model. A Markov model was used (with no half cycle correction in the base case as per the .AF model).
<b>Health states</b>	For both model arms the health states are: 1) Arrhythmia free; 2) Arrhythmia recurrence; 3) Cardiac hospitalisation, mutually exclusive of States 1 and 2; 4) Re-ablation (ablation arm only, once only and within 12 months only), a subset of State 2; 5) Dead. 'Arrhythmia free' and 'arrhythmia recurrence' refer to the arrhythmia being treated by ablation (VT, AFL or AVNRT)
<b>Cycle length</b>	Monthly
<b>Discount rate</b>	5%
<b>Software used</b>	Microsoft Excel 2016 (Redmond, Washington, United States)

Source: Table 4, p16 of the ADAR

AFL, atrial flutter; AVNRT, atrioventricular nodal re-entrant tachycardia; ICD, implantable cardioverter defibrillator; KOL, Key Opinion Leader; QALY, quality-adjusted life year; RCT, randomised controlled trial; VA, ventricular arrhythmia; VT, ventricular tachycardia

In addition to the translation issue assumptions above, the ADAR assumed (consistent with the AF Review) that 5% of cardiac hospitalisations are serious (major complexity) for patients with AFL and AVNRT. For VT+IHD+ICD patients, trial data reported by Sapp (2016)<sup>21</sup> were used to estimate this proportion (79%) based on the proportion of patients having recurrent electrical storms, who often have prolonged hospitalisations and/or experience heart failure.

The Commentary considered that the model structure seems appropriate to the intervention, though if cardiac ablation is considered first-line, the comparator may have less clinical relevance. In some cases, the data available were not appropriate to populate the model. As the authors of the ADAR mention, the mutually exclusive nature of the intervention in not allowing cross-over between arms is different to what might occur in a real situation.

The Commentary also considered that the model structure was based purely on the structure of the AF model, rather than providing justification for VA and non-AF SVT specifically. The Commentary noted that arrhythmia recurrence is extrapolated at the same rate beyond the trial mean/total follow-up of 1 to 5 years. Over the 10-year time horizon of the model, the Commentary considered this could understate the incremental cost-effectiveness ratio (ICER), compared with an assumption of no difference between arms beyond trial follow-up, as the ablation costs are largely up-front, whereas comparator costs continue indefinitely. In addition, the Commentary considered that the one-month cycle length may overestimate the time spent in some health states (e.g. a VT recurrence reverted by an ICD would last much less than one month). The health states have been applied for the full cycle, except for complications, which are considered to last for one week.

<sup>21</sup> Sapp, J, Coyle, K, Parkash, R, et al. (2017). "Cost effectiveness of ventricular tachycardia ablation versus escalation of antiarrhythmic drug therapy in the VANISH trial." *Can J Cardiol*, 33(10): S16-S17.



The Commentary noted the ADARs model assumes that patients in the cardiac ablation arm do not continue AADs or commence AADs. The ADARs KOL provides some support for this assumption in AVNRT patients but acknowledges that AFL patients with concurrent AF may continue AADs, and only 50% of patients with VT+IHD+ICD will stop AADs after cardiac ablation. The applicant claims there are no reliable Australian data available to support this. Continuing AADs following ablation has resource implications and would increase costs over time, potentially leading to a higher ICER.

The overall costs and outcomes, and incremental costs and outcomes, as calculated for the intervention and comparator in the model, using the base case assumptions, are shown in Table 8.

**Table 8 Cost-effectiveness of cardiac ablation versus no ablation in the VA and SVT populations**

Population	Cost – cardiac ablation	Cost – no ablation	Incremental cost	Effectiveness (QALYs) – cardiac ablation	Effectiveness (QALYs) – no ablation	Incremental effectiveness	ICER
<b>VT+IHD+ICD patients</b>	\$24,112 \$22,927	\$15,102 \$13,378	\$9,011 \$9,549	5.19	5.05	0.15	\$61,932 \$65,629
<b>AFL patients</b>	\$18,865 \$18,122	\$12,388 \$11,026	\$6,477 \$7,096	5.72	5.54	0.18	\$35,672 \$39,077
<b>AVNRT patients</b>	\$14,677 \$14,337	\$9,259 \$6,785	\$5,419 \$7,552	6.22	5.62 5.89	0.60 0.33	\$9,029 \$14,022

Source: Table 49 (p.96-97) of ADAR, *with Commentary amendments (changed some costs and outcome data for AVNRT)*

AFL=atrial flutter; AVNRT=atrioventricular nodal re-entrant tachycardia; ICD=implantable cardioverter defibrillator; ICER=incremental cost-effectiveness ratio; IHD=ischemic heart disease; VA=ventricular arrhythmia; VT=ventricular tachycardia; QALY=quality-adjusted life year.

The Commentary considered there is a concern that the ICER for patients undergoing cardiac ablation for VT who have IHD and an ICD (VT+IHD+ICD patients) does not accurately represent the cost-utility of ablation, due to inclusion of both an SLR pooled relative risk that included RCT evidence from conference abstracts, and because of the need for extrapolation for eight of the ten-year time horizon. These issues are addressed in sensitivity analyses.

The overall ICER for cardiac ablation extended to all arrhythmias is summarised in Table 9. The Commentary considered there were several issues with the weighted ICER:

- The weighting in the non-AF SVT group is based on expert opinion only
- The 30% (100% - 20% - 50%) of cardiac ablation for non-AF SVT is presumably for other indications that have not been considered in the economic evaluation.

**Table 9 Weighted incremental cost-effectiveness ratio calculation**

Population	MBS service volume (calendar year = 2018)	Weight	ICER
Atrial fibrillation	5,466	58.3%	\$50,000
Ventricular arrhythmia	644	6.9%	\$61,932 \$65,629
Supraventricular tachycardia (non-AF)	3,270	34.9%	\$16,641 <sup>b</sup> \$21,181
<b>All cardiac ablation</b>	<b>9,380</b>	<b>100.0%</b>	<b>\$39,190</b> <b>\$41,026</b>

Source: Table 6, p17 of ADAR *with Commentary amendments (changed some costs and outcome data for AVNRT)*

AF, atrial fibrillation; AFL, atrial flutter; AVNRT, atrioventricular nodal re-entrant tachycardia; ICER, incremental cost-effectiveness ratio; SVT, supraventricular tachycardia

a Obtained from online MBS services data

b KOL advice suggests that of patients undergoing cardiac ablation for SVT (that is not AF) 20% of procedures are for AFL and 50% are for AVNRT. Therefore, the ICER for SVT is a weighted average of the ICERs for AFL (29%) and AVNRT (71%).

The ADAR considered that the modelled results were most sensitive to the time horizon and discount rate, and (in VT+IHD+ICD patients) the extrapolation of the arrhythmia recurrence probabilities.

In the pre-Evaluation Sub-Committee response, the applicant considered that the model structure under-estimates the cost-effectiveness of cardiac ablation for patients with VT+IHD+ICD. In particular, electrical storm (which is omitted from the model as a specific event) significantly increases mortality:

- A retrospective study of 106 consecutive patients with dilated cardiomyopathy (DCM) and ICDs (Bansch 2000<sup>22</sup>) found that among patients with single VT events, 85.4% survived four years after implantation, in contrast to 45.8% of those with ‘clusters’ of VT events ( $p < 0.004$ ). This represents a significant relative risk of mortality of 1.865 (0.854/0.458) following electrical storm compared with a single VT recurrence
- An RCT of ICD implantation vs. conventional medical therapy (Sesselberg 2007) found that amongst the ICD group ( $n=719$ ) patients who experienced electrical storm had a significantly higher risk of death compared with those with no VT/VF, which persisted after 3 months (hazard ratio [HR] 3.5; 95% CI: 1.5, 4.0;  $p=0.02$ ).

For this response, these data were applied in the data in the economic model to the proportions of patients in each arm reported by Anderson (2019) to have either VT recurrence (39.4% [165/419] vs. 48.9% [185/378]) or electrical storm (17.5% [53/302] vs. 25.7% [78/303]) at a mean follow-up of 2 years. This reduces the ICER for cardiac ablation vs. no ablation from \$61,932 per quality-adjusted life year (QALY) gained to either:

- \$58,926/QALY, applying the RR reported by Bansch (2000); or
- \$56,617/QALY, applying the HR reported by Sesselburg (2007).

#### *Post Evaluation Sub-Committee Addendum*

As per Evaluation Sub-Committee advice, the Commentary presented the ICERs separately for each subpopulation and reporting the ICERs for 2,5 and 10 years (Table 10).

**Table 10 Incremental cost-effectiveness ratios for non-AF cardiac catheter ablation**

	VA+IHD+ICD		AFL <sup>^</sup>	AVNRT <sup>^</sup>
	Appropriate ICD therapies <sup>#</sup>	Appropriate ICD shocks <sup>#</sup>		
<b>2-year time horizon</b>	\$308,566	\$347,802	\$538,178	\$151,890
<b>5-year time horizon</b>	\$101,748	\$118,048	\$120,820	\$37,942
<b>10-year time horizon</b>	\$46,638	\$52,810	\$39,077	\$14,022

AF=atrial fibrillation; AFL=atrial flutter; AVNRT=atrioventricular nodal re-entry tachycardia; VA+IHD+ICD=ventricular arrhythmia + ischaemic heart disease + implantable cardioverter defibrillator.

<sup>#</sup> Note that because the systematic review and meta-analysis by Martinez et al. reports odds ratios, the number of people with an event divided by the total divided by the weighted mean number of months of follow-up has been used to calculate the monthly probability of ICD therapies and shocks for the cardiac ablation and no ablation arms (as in the Commentary). The ICER for a 10-year time horizon is also reported in Table 29 (p 75) of the Commentary (the value for appropriate ICD shocks as \$52,883, due to rounding of transition probabilities in the Commentary value).

<sup>^</sup> These values are identical to those reported in the Commentary in Table 26 (p 73) for the 10-year time horizon and Table 28 (p 75) for the 2- and 5-year time horizons.

<sup>22</sup> Bansch D, Böcker D, Brunn J, et al, 2000, Clusters of ventricular tachycardias signify impaired survival in patients with idiopathic dilated cardiomyopathy and implantable cardioverter defibrillators, *J Am Coll Cardiol*; 36(2): 566-573.

### 13. Financial/budgetary impacts

The ADARs financial analysis used a similar market-share approach to the AF Review and considered the impact of extending the current PL listing for cardiac ablation devices from two main perspectives: private health insurers (PHIs) and the MBS. As per the AF Review, a key uncertainty is whether the exclusion of VA and non-AF SVT from the current PL listing means that patients are missing out on cardiac ablation altogether, or whether some are paying significant out-of-pocket expenses, and whether patients who could be managed in private hospitals currently undergo the procedure in public hospitals. The MBS data only provide an estimate of current private sector utilisation, and as current PHI subsidies for cardiac ablation for AV and non-AF SVT are unknown, the net impact of extending the current PL listing is therefore highly uncertain.

The financial analysis is based on projected MBS usage of cardiac ablation of VA and SVT (all services for MBS items 38293 and 38518; 75% of services for MBS item 38287 for SVT). Conservatively, only the procedural cost of cardiac ablation is applied. The reduced costs to the PBS of AADs (amiodarone) for patients undergoing cardiac ablation is also considered. Other assumptions in the financial analysis are summarised in Table 11. The financial implications summarised in Table 12 assume a 10% increase in MBS services for cardiac ablation of VA and non-AF SVT if the current PL listing is extended to these arrhythmias.

**Table 11 Additional assumptions used in the financial analysis**

Assumption	Input	Source/rationale
Estimated increase in patients undergoing cardiac ablation for VA if the PL listing is extended to these arrhythmias	10%	AF Review (assumption)
Estimated increase in patients undergoing cardiac ablation for SVT if the PL listing is extended to these arrhythmias	10%	AF Review (assumption)
Proportion of MBS services that are privately insured	76%	AF Review (Hospital Casemix Protocol 1 data)
Re-ablation rate	20%	AF Review. This is substantially higher than in the RCTs in Section B. However, the financial analysis is based on procedure numbers (not patient numbers) and this parameter therefore has not impact on the financial estimates.

Source: Table 7, p18 of ADAR

AF, atrial fibrillation; MBS, Medicare Benefits Schedule; PL, Prostheses List; PLAC, Prostheses List Advisory Committee; RFCA, radiofrequency cardiac ablation; SVT, supraventricular tachycardia; VA, ventricular arrhythmia

The Commentary updated the financial estimates for the amended costing inputs from the economic model. The Commentary considered that there is potential for the net cost/year to the MBS to be greater than or less than estimated.

**Table 12 Estimated net impact of the proposed extension to the PL listing – privately insured services**

Assumption	Year 1	Year 2	Year 3	Year 4	Year 5
Number of procedures	316	325	334	342	351
MBS (cardiac ablation procedures)	\$1,152,709	\$1,186,478	\$1,220,247	\$1,254,017	\$1,287,786
PHI (cardiac ablation devices)	\$2,022,730	\$2,078,758	\$2,134,786	\$2,190,814	\$2,246,842
<b>Total cost</b>	<b>\$3,175,439</b>	<b>\$3,265,236</b>	<b>\$3,355,034</b>	<b>\$3,444,831</b>	<b>\$3,534,628</b>
PBS	-\$78,981	-\$81,169	-\$83,356	-\$85,544	-\$87,732
<b>Net cost</b>	<b>\$3,096,458</b>	<b>\$3,184,068</b>	<b>\$3,271,677</b>	<b>\$3,359,287</b>	<b>\$3,446,897</b>

Source: Table 7, pxi of Commentary

MBS=Medicare Benefits Schedule; PBS=Pharmaceutical Benefits Scheme; PHI=private health insurer.

In the pre-Evaluation Sub-Committee response, the applicant noted:

- growth in cardiac ablation services for SVT and VA have been low in recent years, with the 5-year compound annual growth rate (CAGR) being only 0.6% for SVT (MBS item 38287) and 10.6% for VA (MBS items 38293 and 38518) in 2019
- the 5-year CAGR for VA is very similar to that for AF (10.3%). Therefore, an assumed 10% increase in demand additional to current growth is expected to be an upper limit (or to over-estimate) for the growth in private sector demand for cardiac ablation in any indication.

#### 14. Key issues from Evaluation Sub-Committee for MSAC

Evaluation Sub-Committee key issue	Evaluation Sub-Committee advice to MSAC
Safety	Catheter ablation is likely to have superior safety compared with anti-arrhythmic drugs.
Clinical effectiveness – supraventricular tachycardia	The intervention is effective in reducing arrhythmia recurrence.
Clinical effectiveness – ventricular arrhythmia	The evidence base should be limited to published studies so that the effect of bias can be assessed. Therefore, studies with abstracts only should be excluded from the evidence base. Outcome for ventricular arrhythmia recurrence was not statistically significant when conference abstracts are excluded.
Registry of outcomes post-cardiac ablation to evaluate individual and laboratory performance	Apart from QA/QI as part of good clinical governance, a registry could be used to provide transparent feedback to patients and private health insurers to support informed decision-making.
Cost-effectiveness	Overall, the intervention is cost-effective, within each type of arrhythmia over a 10-year horizon. But, in the shorter term, upfront costs are calculated and result in a larger ICER, which is not cost-effective. Given the different subpopulations of age and scarce evidence from literature, Evaluation Sub-Committee recommends separating the ICERs and considering time horizons of 2, 5 and 10 years.  Evaluation Sub-Committee also noted the comparator (no cardiac ablation) may be partially, but not completely, replaced by catheter ablation as it is possible for patients to still require AADs after ablation
Data on uptake in private hospitals	The MBS items 38290 and 38287 were only updated in 2019. Therefore, a review may be needed in 1–2 years.

## ESC discussion

The Evaluation Sub-Committee noted that this Application 1622 is seeking to expand the conditions of listing to include patients with symptomatic ventricular arrhythmia (VA) or non-Atrial Fibrillation supraventricular tachycardia (non-AF SVT). Currently, the Prostheses List (PL) includes cardiac ablation devices that are only used for specified procedures (MBS Items 38287 or 38290) for the treatment of atrial fibrillation (AF).

The Evaluation Sub-Committee noted that this submission does not seek to change clinical practice, since cardiac ablation is already standard practice for patients with these classes of arrhythmia. Rather, it seeks to extend private health insurance funding for cardiac ablation devices from patients with AF to these additional arrhythmia populations. That is, this application is for expansion into current items, with the aim of reducing burden on the public system.

The Evaluation Sub Committee noted that the evidence base is eight individual studies and one meta-analysis. The oldest three of these reports are conference abstracts, which have not been published in peer-review journals, which the Evaluation Sub-Committee recommended be removed from the analysis. The Evaluation Sub-Committee noted that, in the pre-meeting response, the applicant argued that the conference abstracts are relevant. However, the Evaluation Sub-Committee noted that including the abstracts significantly changes the outcomes for the VA population.

As noted in the commentary, the assessment of safety reported in the assessment report is consistent with the AF Review. However, the AF Review was a rapid evidence assessment and is less rigorous than that specified within MSAC assessment guidelines. The Evaluation Sub-Committee agreed with the safety data provided in the commentary, which it considered to be more reliable than that provided in the assessment report because it included additional data, suggesting rates of procedural complications of 8–10% for VA, 2% for AFL and less than 2% for other SVRTs. As AADs, particularly amiodarone, have high rates of adverse events with ongoing administration, catheter ablation is likely to have superior safety in comparison.

In terms of clinical effectiveness, the Evaluation Sub-Committee agreed with the commentary that:

For VA, the conclusion of superior effectiveness was appropriate, but the statistically significant differences were for the outcomes of appropriate implantable cardioverter-defibrillator (ICD) therapies and electrical storm. The outcome of arrhythmia recurrence was not statistically significant when the identified conference abstracts were excluded and therefore there is uncertainty about this outcome. ICD therapies and electrical storm are considered important outcomes for this population, despite not being specified in the PICO.

For atrial flutter (AFL), there is evidence of superior effectiveness, but the evidence presented was limited; the magnitude of the effect (in particular, for AFL-specific recurrence) was large. The effect was reduced if other arrhythmias, in particular AF, are considered in the outcome.

For atrioventricular nodal re-entry tachycardia (AVNRT), there is evidence of superior effectiveness based on a single, small RCT; the magnitude of the effect was large.

No evidence was presented for other SVT populations.

The Evaluation Sub-Committee noted that the effectiveness for cardiac ablation therapy is less established than for AF and requires operator training to establish skill and experience – this is particularly relevant for the VA population. Given the availability of super-specialisation training programs for cardiac electrophysiology, the Committee suggested that a registry of outcomes post-ablation be established, to capture individual and laboratory performance. Such a registry could be used to provide transparent feedback to patients and private health insurers, and to support informed decision-making.

In terms of cost effectiveness, the Evaluation Sub-Committee noted the different subpopulations in terms of age as well as the scarce evidence from literature, and therefore recommended calculating separate incremental cost-effectiveness ratios (ICERs) for the VA, AFL and all remaining tachycardia groups. The Committee agreed that having 2- and 5-year time horizons was reasonable. With the older age groups, the Committee considered that a 10-year follow-up may overestimate the life years gained. However, it was noted that some young people have VAs. Therefore, the Committee suggested that remodelling should include 2- and 5-year time horizons, and an additional sensitivity analysis should consider a 10- year time horizon. As stated above, the Committee considered that this remodelling should not include the Anderson data based on conference abstracts.

The Evaluation Sub-Committee noted that the weighted cost was based on expert opinion and is higher than the listed cost, but that the model used a lower cost. While the weighted cost is feasible, the Committee questioned whether it necessary or logical. The Committee noted that the assessment group will investigate this further and liaise with the Department and MSAC out of session.

The Evaluation Sub-Committee noted that that the devices required for MBS item numbers 38290 and 38287 were only listed on the PL in 2019, so current data and growth may not potentially reflect expected growth and recommended that the Department consider reviewing usage in 1–2 years.

#### **15. Other significant factors**

Nil

#### **16. Applicant comments on MSAC's Public Summary Document**

The applicant had no comment.

#### **17. Further information on MSAC**

MSAC Terms of Reference and other information are available on the MSAC Website: [visit the MSAC website](#)